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CHEMICAL RESEARCH, DEVELOPMENT & ENGINEERING CENTER

CRDEC-TR-88083

# ESTIMATION OF REACTIVITY BASED UPON STERIC FACTORS: AMIDIZATION OF ESTERS



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March 1988

U.S. ARMY ARMAMENT MUNITIONS CHEMICAL COMMAND

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# REPORT DOCUMENTATION PAGE

| | |
|---|---|
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| 2a. SECURITY CLASSIFICATION AUTHORITY | 3 DISTRIBUTION / AVAILABILITY OF REPORT<br>Approved for public release; distribution is unlimited. |
| 2b. DECLASSIFICATION / DOWNGRADING SCHEDULE | |
| 4. PERFORMING ORGANIZATION REPORT NUMBER(S)<br>CRDEC-TR-88083 | 5. MONITORING ORGANIZATION REPORT NUMBER(S) |
| 6a. NAME OF PERFORMING ORGANIZATION<br>CRDEC<br>6b. OFFICE SYMBOL (If applicable)<br>SMCCR-RSP-C | 7a. NAME OF MONITORING ORGANIZATION |
| 6c. ADDRESS (City, State, and ZIP Code)<br>Aberdeen Proving Ground, MD 21010-5423 | 7b. ADDRESS (City, State, and ZIP Code) |
| 8a. NAME OF FUNDING / SPONSORING ORGANIZATION<br>CRDEC<br>8b. OFFICE SYMBOL (If applicable)<br>SMCCR-RSP-C | 9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER |
| 8c. ADDRESS (City, State, and ZIP Code)<br>Aberdeen Proving Ground, MD 21010-5423 | 10. SOURCE OF FUNDING NUMBERS<br>PROGRAM ELEMENT NO. / PROJECT NO. 14N463615 / TASK NO. DE762X / WORK UNIT ACCESSION NO. |

11. TITLE (Include Security Classification)

Estimation of Reactivity Based Upon Steric Factors: Amidization of Esters

12. PERSONAL AUTHOR(S)
Famini, George R., and Leonard, Joseph M., Ph.D.

| 13a. TYPE OF REPORT | 13b. TIME COVERED | 14. DATE OF REPORT (Year, Month, Day) | 15. PAGE COUNT |
|---|---|---|---|
| Technical | FROM 87 May TO 87 Jul | 1988 March | 16 |

16. SUPPLEMENTARY NOTATION

| 17. COSATI CODES | | |
|---|---|---|
| FIELD | GROUP | SUB-GROUP |
| 20 | 05 | |
| | | |

18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
Molecular modeling, Methacrylates, Computational chemistry, polymers, Molecular graphics, Esters, mjm

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

Using capabilities of the Molecular Modeling Analysis and Display System (MMADS), we examined and modeled the relative reactivities of i-butyl acetate and poly i-butyl methacrylate to amidization. Due to visualization and computational constraints, the polymer has been approximated as a tetramer. The amine is sterically constrained from reaching the reactive centers of the polymer/tetramer model but freely reacts with the analogous site in the monomer. This reaction is in agreement with experimental results using both the monomer and polymer of t-butyl acetate.

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|---|---|
| 20. DISTRIBUTION / AVAILABILITY OF ABSTRACT<br>☒ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT. ☐ DTIC USERS | 21. ABSTRACT SECURITY CLASSIFICATION<br>UNCLASSIFIED |
| 22a. NAME OF RESPONSIBLE INDIVIDUAL<br>SANDRA J. JOHNSON | 22b. TELEPHONE (Include Area Code)<br>(301) 671-2914<br>22c. OFFICE SYMBOL<br>SMCCR-SPS-T |

DD FORM 1473, 84 MAR 83 APR edition may be used until exhausted. All other editions are obsolete.

SECURITY CLASSIFICATION OF THIS PAGE
UNCLASSIFIED

## PREFACE

The work described in this report was authorized under Project No. 14N463615DE762X. This work was started in May 1987 and completed in July 1987.

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# ESTIMATION OF REACTIVITY BASED UPON STERIC FACTORS: AMIDIZATION OF ESTERS

## 1. INTRODUCTION

To determine if two compounds will react based upon purely steric parameters is fairly easy to conceptualize. In principle, it should be possible to "map" the reactive site of the larger reactant such that the size of the smaller reactant is taken into effect. In this way, the steric fit of the two reactants can be examined, and the reactivity based upon steric grounds can be estimated.

The particular reaction examined was the amidization of i-butyl acetate with i-propyl amine. The reactants are shown in Figure 1, i-propyl amine on the left and i-butyl acetate on the right. Each atom is represented as a sphere with a radius equal to the corresponding van der Waals radius. In this representation, nitrogen is blue, carbon grey, oxygen red, and hydrogen is white. The end products of the reaction are displayed in Figure 2, i-propyl acetamide on the left and i-butyl alcohol (represented as the oxy anion) on the right.

One particular option within the Molecular Modeling Analysis and Display System (MMADS) at Research Directorate, U.S. Army Chemical Research, Development and Engineering Center (CRDEC), lends itself very well to this type of study. This routine, the Connolly Solvent Accessible Surface Algorithm,[1] calculates the surface of a substrate molecule in contact with a solvent of a given radius. For a reaction to take place, the i-propyl amine must reach the active site of the i-butyl acetate (a carbonyl carbon). This routine can be used to determine if it is sterically possible for a reaction to occur.

As with all modeling efforts, it is impossible (both in terms of computer time necessary and viewability) to duplicate the exact system being examined. Therefore, approximations have been made. Using an empirical optimization technique such as molecular mechanics permits large molecules (between 100 to 200 atoms) to be sterically optimized in a minimal amount of time. Using pictorial techniques, the size of the structure must be kept reasonable to permit the eye to observe the regions of interest. For these reasons, a tetramer of the i-butyl methacrylate was considered sufficient to model the polymer interactions but was small enough to allow for ready identification of the active sites.

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[1]Connolly, M., Science Vol. 221, p. 709 (1981).

## 2. EXPERIMENTAL PROCEDURE

The structures of i-butyl acetate, the corresponding tetramer, and i-propyl amine were geometrically optimized using the Allinger molecular mechanics algorithm.[2] The solvent accessible surface was calculated using the Connolly algorithm.[1] Both routines are resident in the MMADS, running on a VAX computer under the VMS operating system at CRDEC.[3] All photographs were taken from an Adage 3000 Color Raster Display using a Dunn 635 camera.

## 3. RESULTS

This investigation was to determine if poly i-butyl methacrylate would undergo amidization. Figure 3 shows the optimized structure of the i-butyl acetate tetramer. The color scheme of the previous figures is used, except that the active site (the carbonyl carbon) is green for clarity. By assuming that the i-propyl amine molecule can be approximated as a sphere with a radius of 3.616 A (the effective van der Waals radius of the molecule), the solvent accessible surface can be generated for the potential reaction pair, i-propyl amine and poly i-butyl methacrylate. This surface is shown in Figure 4. The presence of green dots, denoting that the carbonyl carbon can be "touched" by the i-propyl amine, is an indication that the reaction could occur based upon steric constraints. As seen from the figure, no green dots are visible, indicating that poly i-butyl methacrylate would be unreactive towards i-propyl amine. This agrees with experimental results.

Experimental results show, however, that the monomer unit of i-butyl acetate readily undergoes amidization. Therefore, if this model is to be successful in prediciting steric based reactivity, it must also be able to predict that this reaction can occur. The monomer unit is shown in Figure 5 using the same color scheme as Figure 3. The solvent accessible surface was calculated using the same conditions as the polymer, producing the results shown in Figure 6. The significant number of green dots on the surface indicates that the carbonyl carbon in the monomer is accessible to the i-propyl amine; and therefore, a reaction can occur.

## 4. CONCLUSION

The study shows that it is possible to use computational techniques to rationalize apparently anomalous experimental results. In reactions where steric constraints are the primary factors, this methodology should be applicable.

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[2]Allinger, N., and Burkert, V., ACS Monograph 177, American Chemical Society, Washington, DC (1982).

[3]Leonard, J., A User's Guide to the Molecular Modeling Analysis and Display System (MMADS), CRDEC-TR-86039, U.S. Army Chemical Research, Development and Engineering Center, Aberdeen Proving Ground, MD, May 1986, UNCLASSIFIED Report.

First, the solvent accessible surface algorithm assumes that the solvent molecule can be represented as a sphere. This assumption is not completely valid, and the results become less useful as the solvent molecules become less spherical. However, if the solute is much larger than the solvent, the approximation will hold. Second, this model addresses only the steric factors in a reaction, completely ignoring the electronic factors. Although this may not be important in this reaction, electronic interactions may be the rate limiting step in other reactions.

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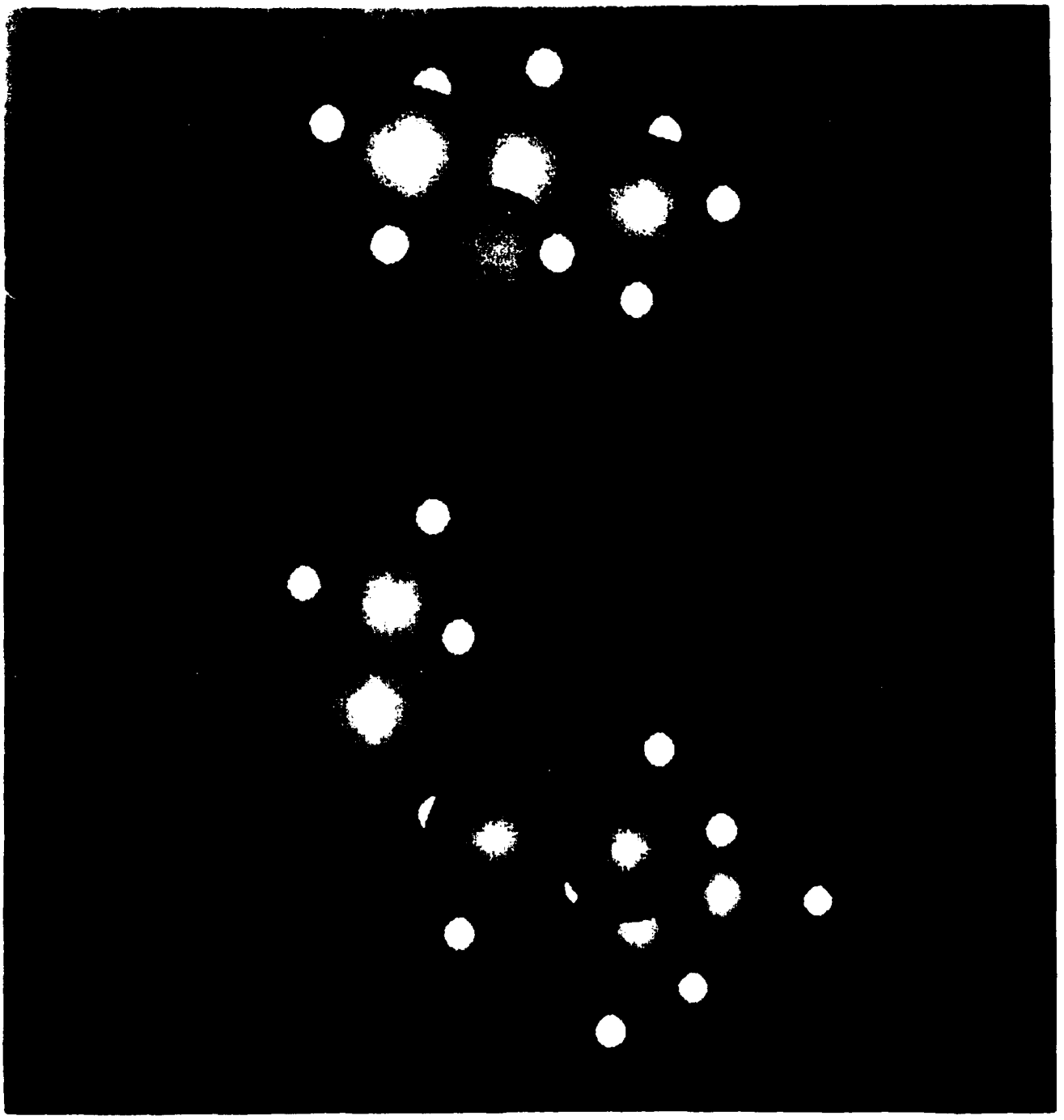

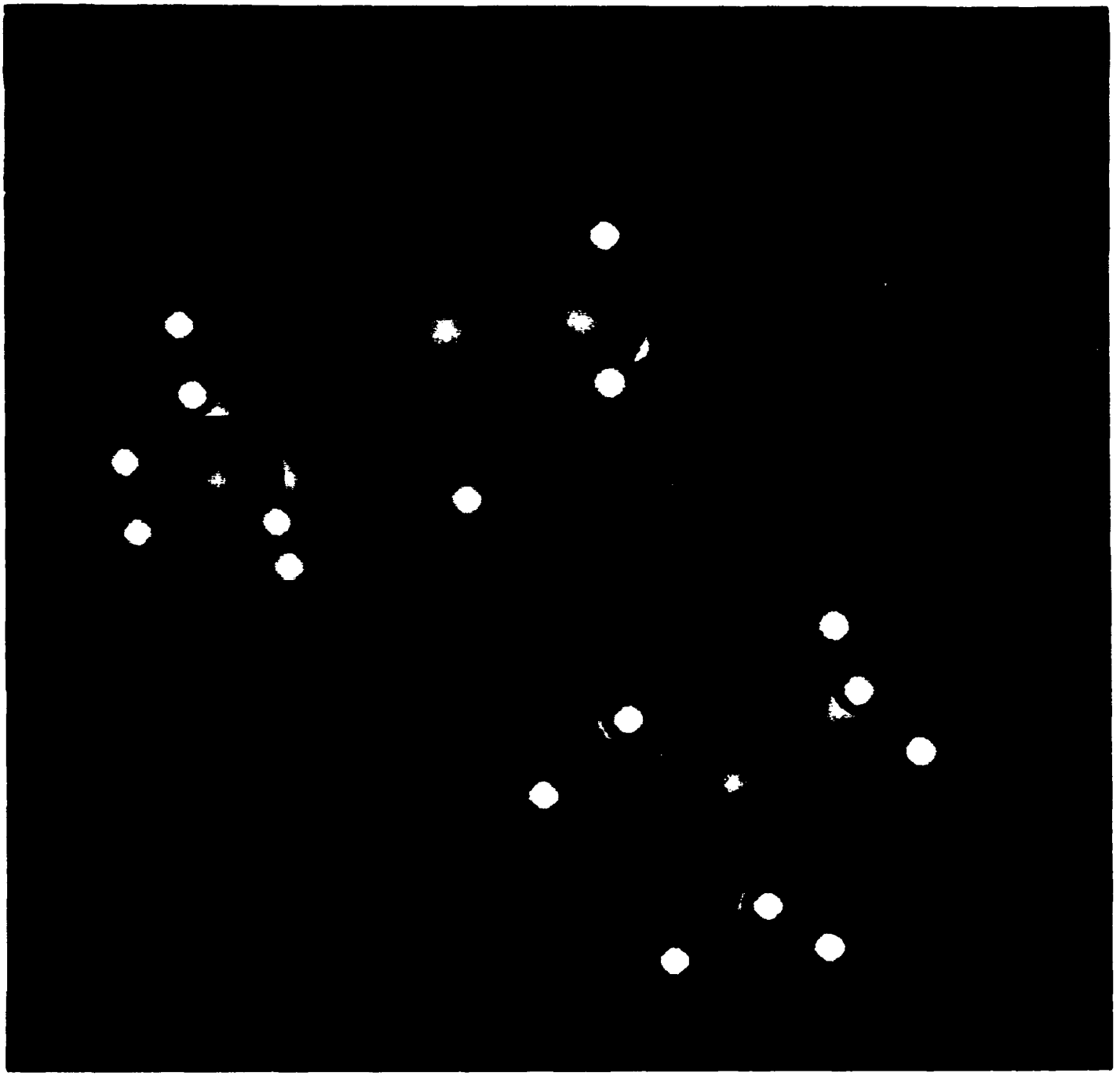

Figure 2. Amidization Products

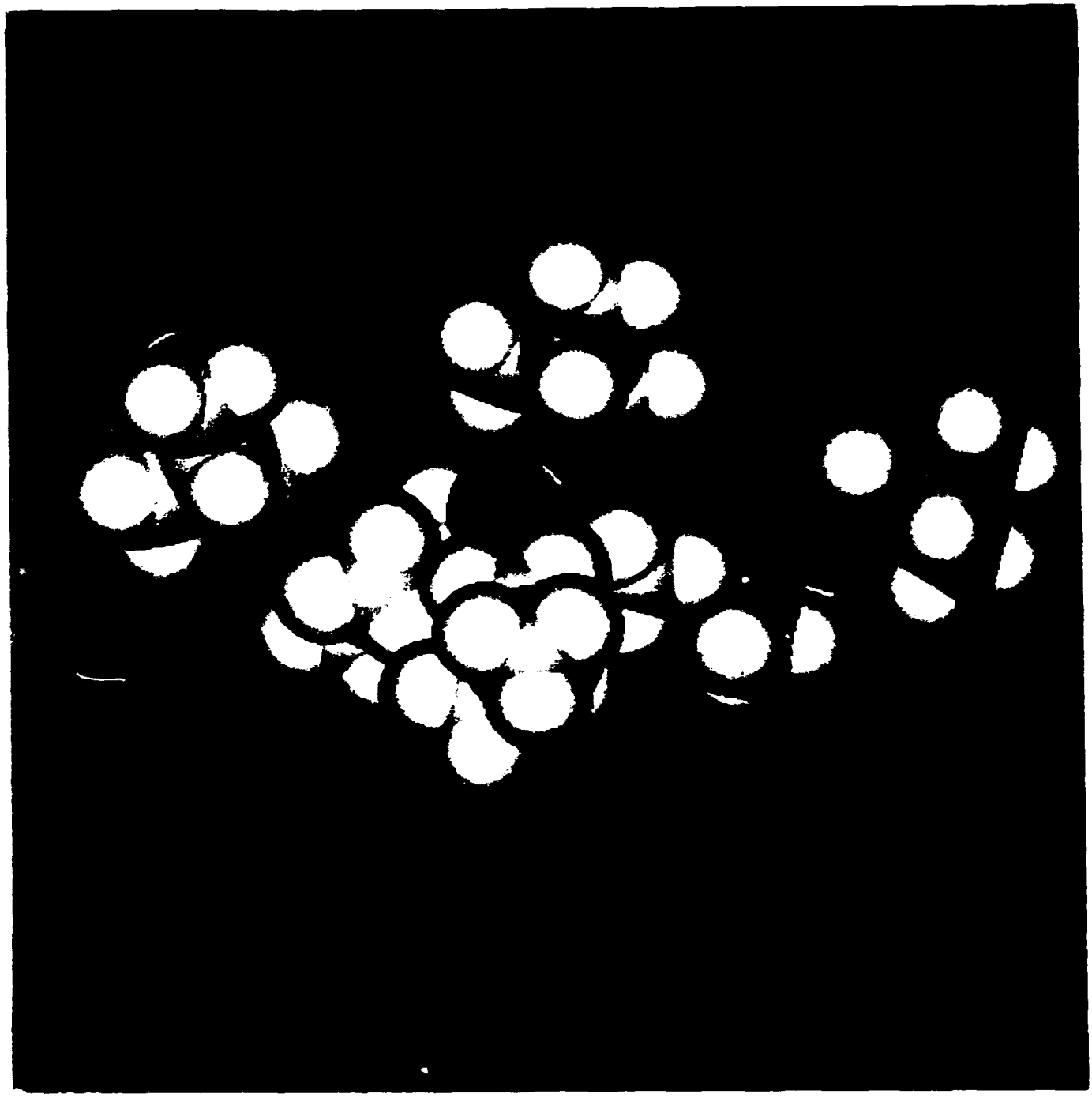

Figure 3. Tetramer of i-Butyl Acetate (space fill)

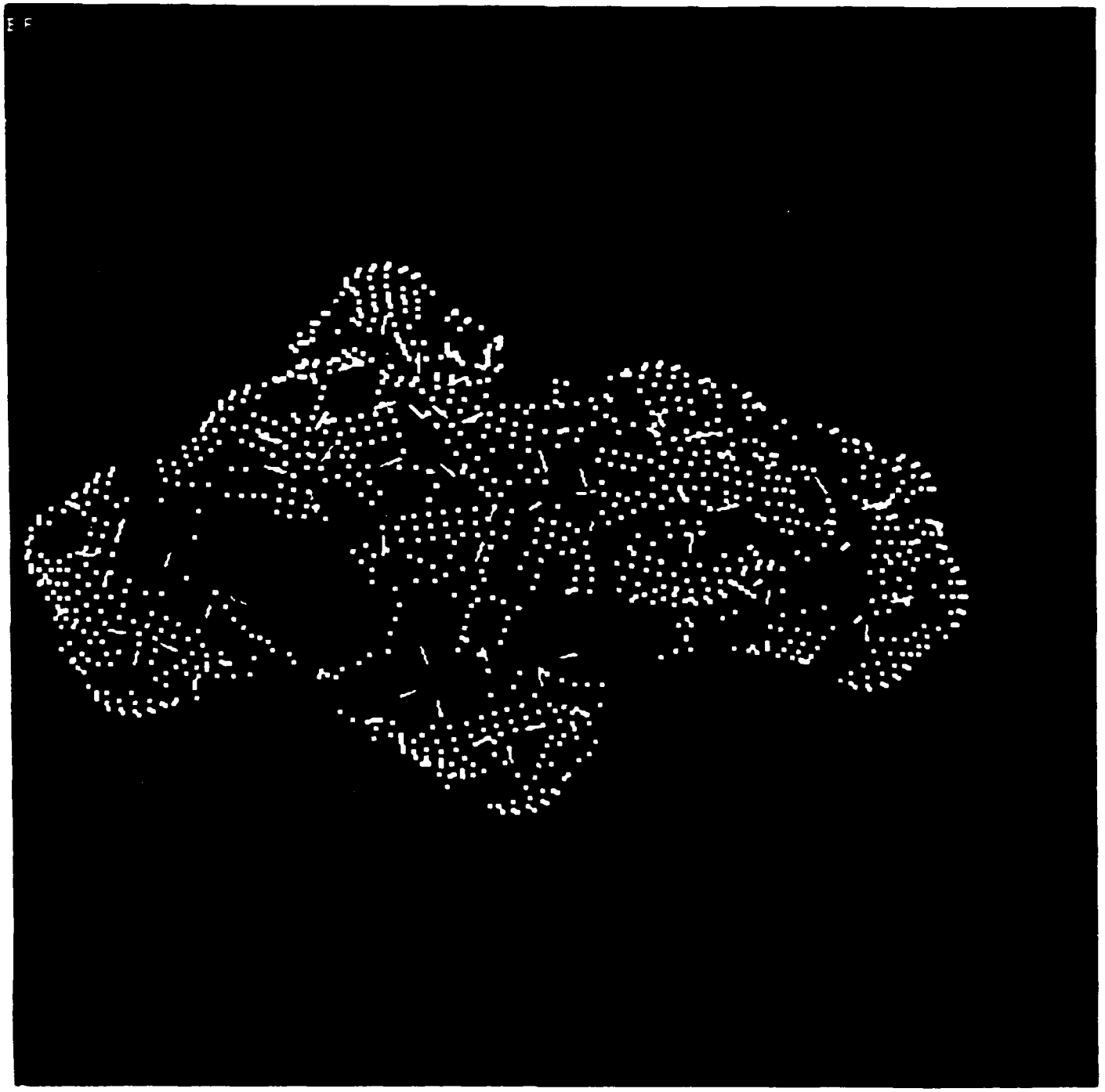

Figure 4. Solvent Accessible Surface of i-Butyl Acetate Tetramer

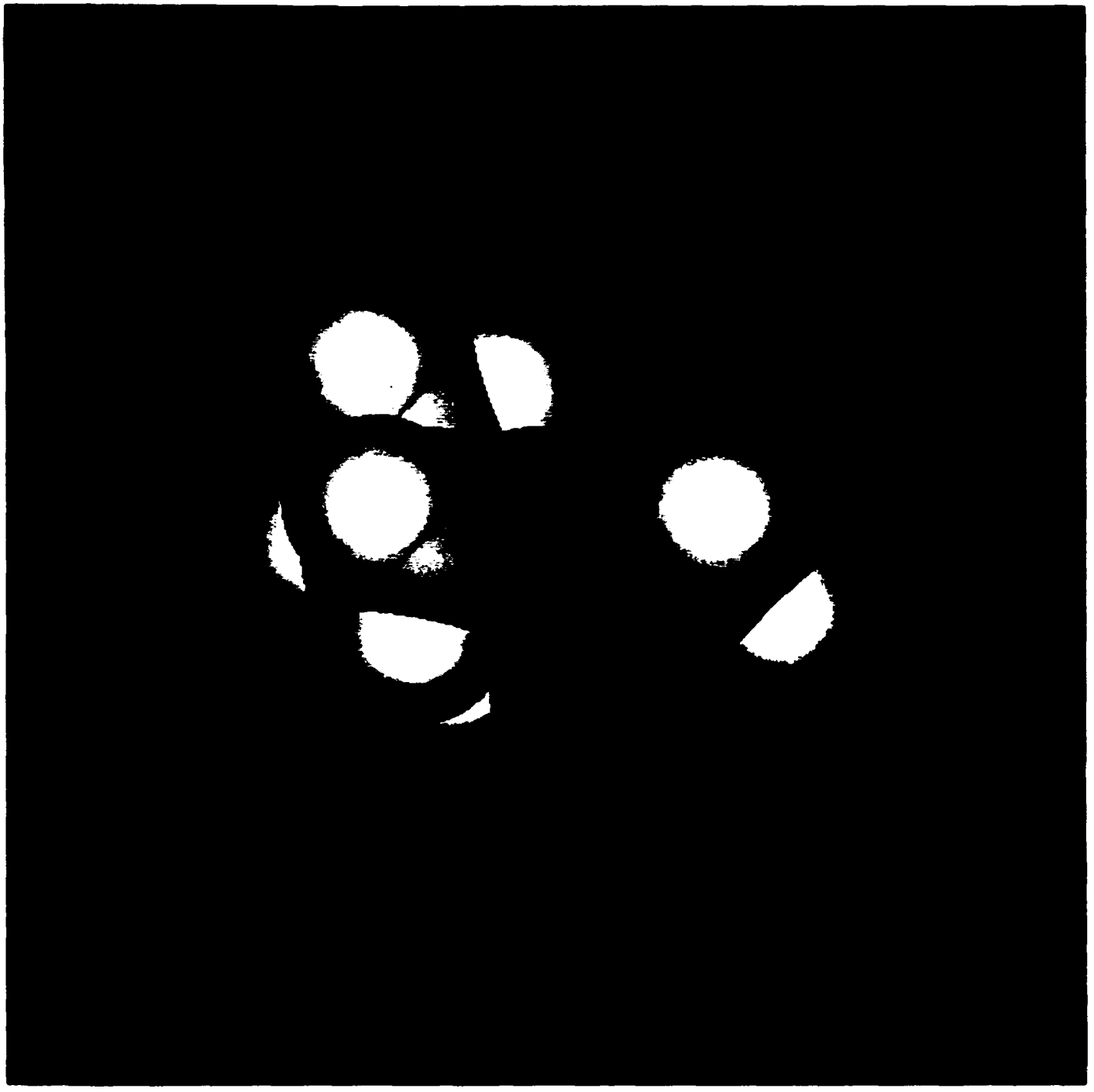

Figure 5. i-Butyl Acetate (space fill)

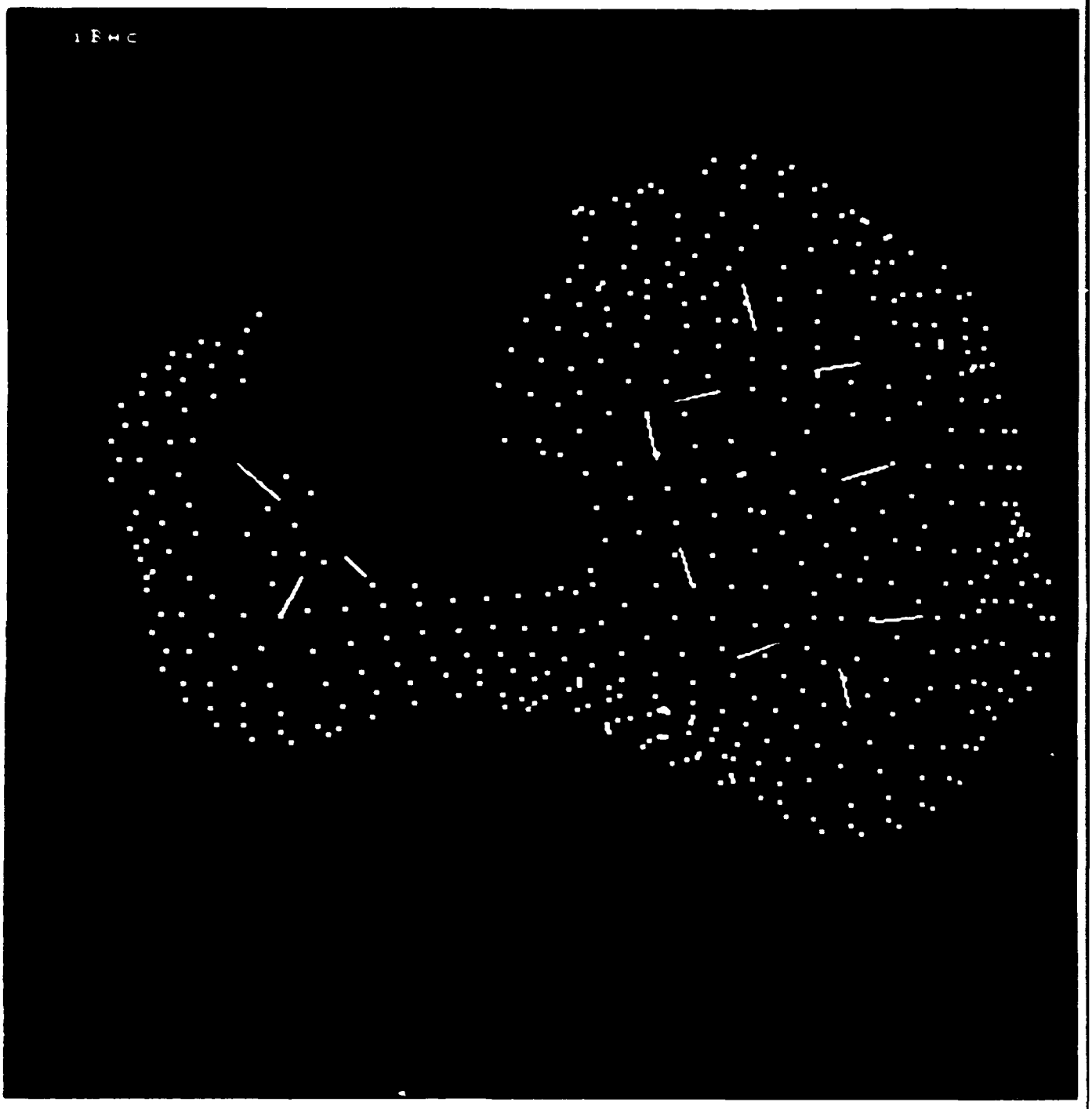

Figure 6. Solvent Accessible Surface of i-Butyl Acetate